Bio-Orthogonally Crosslinked, Engineered Protein Hydrogels with Tunable Mechanics and Biochemistry for Cell Encapsulation.

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Public Summary:
Covalently-crosslinked hydrogels are commonly used as 3D matrices for cell culture and transplantation. However, the crosslinking chemistries used to prepare these gels generally cross-react with functional groups present on the cell surface, potentially leading to cytotoxicity and other undesired effects. Bio-orthogonal chemistries have been developed that do not react with biologically relevant functional groups, thereby preventing these undesirable side reactions. However, previously developed biomaterials using these chemistries still possess less than ideal properties for cell encapsulation, such as slow gelation kinetics and limited tuning of matrix mechanics and biochemistry. Here, engineered elastin-like proteins (ELPs) are developed that cross-link via strain-promoted azide-alkyne cycloaddition (SPAAC) or Staudinger ligation. The SPAAC-crosslinked materials form gels within seconds and complete gelation within minutes. These hydrogels support the encapsulation and phenotypic maintenance of human mesenchymal stem cells, human umbilical vein endothelial cells, and murine neural progenitor cells. SPAAC-ELP gels exhibit independent tuning of stiffness and cell adhesion, with significantly improved cell viability and spreading observed in materials containing a fibronectin-derived arginine-glycine-aspartic acid (RGD) domain. The crosslinking chemistry used permits further material functionalization, even in the presence of cells and serum. These hydrogels are anticipated to be useful in a wide range of applications, including therapeutic cell delivery and bioprinting.

Scientific Abstract:
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